REMARKS

I. Status of Claims

Claims 1-12, 14, and 18-22 are pending in this application. Claim 1 has been amended to correct a misspelled word ("alkoxycarbonyl") and to further clarify the nature of the invention by adding "and" between "independently" and "optionally" in the definition of R_1 and R_2 at paragraph (a)(ii). Claim 10 has been amended to correct a misspelled word ("alkoxycarbonyl.") No new matter has been added by the present amendments.

II. Restriction Requirement

The Examiner made the Restriction Requirement of November 14, 2007, final. *See* Office Action at 2. The Examiner withdrew claims 12, and 18-22 from consideration on the merits in this application. The Examiner argues that Applicants defined the special technical feature linking the claims as being the 4-aminothieno[2,3-d]pyrimidine-6-carbonitrile core. Applicants respectfully disagree with the Examiner's interpretation of the special technical feature of the invention and the disclosure in the reference cited, EP 0 447 891.

Foremost, Applicants point out that the response to the Restriction Requirement made it clear that "the special technical feature linking the claims is not limited to the [4-aminothieno[2,3-d]pyrimidine-6-carbonitrile core], but rather encompasses the position and identity of the radicals R_1 to R_4, which are also part of the structure of compounds of formula (I)." Response to Restriction Requirement filed on December 13, 2007, at 2. In particular, EP 0 447 891 teaches different substituents for the compounds of formula I disclosed therein. For example, R^3 is "chlorine, bromine, hydroxyl, or mercapto with the

proviso that R^2 is not hydroxyl when R^3 is bromine, and R^3 is not hydroxyl when R^4 is alkocycarbonyl or carboxyl." *See* Abstract of Canadian Application No. 2038521, which is member of the same patent family of the German-language EP 0 447 891, and which Applicants believe discloses the same subject matter as EP 0 447 891. In contrast, the present application teaches that R_4, which corresponds to R^3 of EP 0 447 891 "represents a hydrogen atom, an alkyl group or an aryl group." *See* claim 1. Accordingly, EP 0 447 891 does not teach the special technical feature of the instant invention.

Further, Applicants respectfully remind the Examiner of the rejoinder procedure of M.P.E.P. § 821.04. This section of the M.P.E.P. provides that claims directed to nonelected processes of making or using a product are subject to rejoinder with claims drawn to that product once the product is found patentable. *See also In Re Ochiai*, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 77 F.3d 422, 37 USPQ2d 1663 (Fed. Cir. 1996). The M.P.E.P. requires that "[i]n order to be eligible for rejoinder, a claim to a nonelected invention must depend from or otherwise require all the limitations of an allowable claim." *Id.* Applicants point out that the claims of Groups II-V, which are directed to methods of making a compound as claimed in claim 1, methods of treating comprising administering a compound as claimed in claim 1, combination product comprising a compound as claimed in claim 1, and a composition comprising a compound as claimed in claim 1, respectively, comply with this provision. Therefore, these claims are eligible for rejoinder once the compounds of claim 1 are found patentable. Accordingly, Applicants respectfully request that all pending claims be examined in this application.

III. Claim Objections

On page 3 of the Office Action, the Examiner objected to claims 1 and 10. With regards to the misspelling of "alkoxycarbonyl," Applicants have amended the claims correcting the informality as required by the Examiner. Accordingly, Applicants respectfully request that this objection be withdrawn.

The Examiner also takes issue with the phrase, "alkyl and alkylene groups, wherein each alkyl and alkylene ,qroup [*sic*] is independently optionally substituted by one or more ...." *Id.* The Examiner seems to propose to delete the term "independently" from the claim language, as well as to modify the language of the recited Markush group. The Examiner has provided no explanation in support of the proposed amendment and Applicants fail to see the source of the "informality."

However, to further clarify that each of the recited groups can be optionally substituted, independently of each other, Applicants have amended claim 1 to recite that each group "is independently and optionally" substituted.

Applicants believe that the language of the Markush group the Examiner proposes to amend is proper and definite. Therefore, in the absence of an explanation from the Examiner as to the nature of the deficiency in such language, Applicants have not amended claim 1 in that regard.

IV. Rejections under 35 U.S.C. § 112

A. Second paragraph

The Examiner has rejected claims 1-10, and 14 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner states that "[t]he term "acyl" is vague throughout the claims ... and there is no one, generally accepted, definition."

Office Action at 3-4. Applicants respectfully disagree and traverse for at least the following reasons.

As an initial matter, one of skill in the art would know that the term "acyl" refers to "[a]n organic acid group in which the OH of the carboxyl group is replaced by some other substituent (RCO-)." Hawley's Condensed Chemical Dictionary, fifteenth edition, at 23 (definition of acyl; copy enclosed for Examiner's convenience) (underlining added). Thus, the examples that the Examiner recites in the Office Action at page 4, i.e., "nitro group", "Cl", "OH," do not meet this definition and would not be considered as encompassed by "acyl" by one of ordinary skill in the art. Moreover, the term, "acyl" is clearly defined within the specification:

> As used herein, the term acyl embraces optionally substituted, linear or branched radicals having 1 to 20 carbon atoms or, preferably 1 to 12 carbon atoms attached to a carbonyl radical. More preferably acyl radicals are "lower acyl" radicals having 2 to 8, preferably 2 to 6 and more preferably 2 to 4 carbon atoms. Thus, it is typically a radical of formula -COR. An acyl group is typically unsubstituted.
>
> Preferred optionally substituted acyl radicals include acetyl, propionyl, butiryl, isobutiryl, isovaleryl, pivaloyil, valeryl, lauryl, myristyl, stearyl and palmityl.

See Specification at paragraphs [0057]-[0058] of the published application (emphasis added).

Thus, for at least the reasons stated above, Applicants submit that the claim language with regards to the term "acyl" is definite, and respectfully request the withdrawal of the Examiner's rejection.

Further, the Examiner takes issue with claim 2, stating that "[t]here is insufficient antecedent basis for [a] limitation in the claim." *Id.* at 4. Specifically, the Examiner

argues that the limitation "wherein each C_1-C_4 alkyl group is independently ...substituted by one hydroxyl group" for R_1 and R_2 lacks antecedent basis. Applicants respectfully traverse this rejection.

Applicants point out that the claims are interpreted, *inter alia*, in light of the disclosure in the specification. M.P.E.P. § 2173.02. The specification indicates that "[a]s used herein the term alkyl embraces optionally substituted . . . radicals," and further explains that "[t]he substituent(s) are typically halogen atoms, . . . and hydroxyl . . . radicals." Specification at ¶¶ [0030] to [0033]. Therefore, the recitation of "alkyl" as a substituent for the ring optionally formed by R_1 and R_2 in claim 1, from which claim 2 depends, provides the necessary antecedent basis for the language in claim 2. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The Examiner also rejects claim 11 for "insufficient antecedent basis for [the R_3 substituent for species 3, 4, and 8-11] limitation in the claim." *Id.* Applicants respectfully traverse this rejection for at least the reason that claim 1, from which claim 11 depends, defines R_3 as encompassing the R_3 substituents disclosed for species 3, 4, and 8-11 in claim 11.

In particular, the compounds the Examiner has referred to as "species 3" (4-(6-Cyano-4-diethylamino-5-methylthieno[2,3,d]pyrimidin-2-yl)-benzoic acid methyl ester), "species 4" (4-[6-Cyano-4-(ethylmethylamino)-5-methylthieno[2,3,d]pyrimidin-2-yl]-benzoic acid methyl ester), "species 8" (methyl 4-(6-cyano-5-methyl-4-morpholin-4-ylthieno[2,3,d]pyrimidin-2-yl)benzoate), "species 9" (methyl 4-[6-cyano-5-methyl-4-(4-methylpiperazin-1-yl)thienol[2,3,d]pyrimidin-2-yl]benzoate), "species 10" (methyl 4-[6-cyano-4-(dimethylamino)-5-methylthienol[2,3,d]pyrimidin-2-yl]benzoate, and "species

11" (methyl 4-[6-cyano-4-[(2-hydroxyethyl)(methyl)amino]-5-methylthieno[2,3,d]pyrimidin-2-yl]benzoate) all possess, as the R_3 variable, a group that is within the definition of R_3 in claim 1. That is, all compounds cited by the Examiner have an R_3 group of formula $-(CH_2)_n-G$, wherein n is equal to 0, and G is a monocyclic aryl group substituted with a methoxycarbonyl group.

Accordingly, there is sufficient antecedent basis for the R_3 substituent for species 3, 4, and 8-11. For at least these reasons, Applicants respectfully request that this rejection be withdrawn.

Finally, the Examiner rejects claim 4 arguing that "[t]here is insufficient antecedent basis for this limitation [dialkylamino in the definition of R_2] in the claim." *Id.* Applicants respectfully traverse this rejection for at least the reason that claim 1, from which claim 4 depends, recites that R_2 can be chosen from "alkyl, alkenyl, and alkynyl groups, wherein each alkyl, alkenyl and alkynyl group is independently optionally substituted by one or more substituents chosen from halogen atoms ... and mono- and di-alkylamino groups." *Id.* Thus, Applicants submit that the limitation for R_2 as a "dialkylamino" in claim 4, is clearly within the scope of claim 1, as R_2 can be chosen from an alkyl group substituted by a mono-alkylamino group, which provides sufficient antecedent basis for the R_2 substituent in claim 4. For these reasons, Applicants respectfully request that this rejection be withdrawn.

B. First paragraph

Claims 1-10, and 14 are rejected for allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112 for the reasons set forth at pages 4-7 of the Office Action. The Examiner asserts that "[t]he specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims." Specifically, the Examiner argues that "[t]he specification does not provide any support for the synthesis of compounds of Formula I, wherein R_1 [sic R_4] is H, alkyl other than methyl or aryl," and further argues that [t]he availability of starting materials that is needed to prepare the invention as claimed is at issue here." *Id.* Applicants respectfully disagree and traverse the rejection for at least the following reasons.

To satisfy the enablement requirement, the specification must enable a person of ordinary skill in the art to practice the claimed invention without undue experimentation. *See, e.g.*, M.P.E.P. §2164.01. Thus, the test is whether it would require undue experimentation to practice the invention. *See generally, Atlas Powder v. E.I. Du Pont de Nemours & Co.* 750 F.2d 1569, 224 U.S.P.Q. 409 (Fed. Cir. 1984). Furthermore, M.P.E.P. § 2164.06 states that "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." M.P.E.P. § 2164.06 (citing *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)) (emphasis added).

Despite taking into account each of the individual *Wands* factors, the Examiner has failed to consider all the evidence related to each of the *Wands* factors. Each of the points the Examiner raised is responded to in turn below and underscores how the Examiner has not established, through adequate evidence and reasoning, a *prima facie* case of nonenablement.

1. Breadth of claims

"As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims." M.P.E.P. § 2164.08.

Here, in determining the breadth of a relevant claim to the enablement of the disclosure, the Examiner fails to set forth how the disclosure does not enable one skilled in the art to make and use the entire scope of the claimed invention without undue experimentation, and only states that "[o]wing to the range of many variables, billions of substituted thieno[2,3-d]pyrimidines are embraced." Office Action at 5. Applicants respectfully assert that formula (I) is a genus of compounds for which several representative species are disclosed in the specification. This type of representation is widely used in patents disclosing similar genus-species relationships. The mere fact that the claimed formula (I) represents multiple chemical species does not by itself support lack of enablement of the claims. *See, e.g.*, M.P.E.P. § 2164.08.

2. Nature of the invention and level of predictability in the art

The Examiner states that "[i]t is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor." *Id.* at 5 However, the relationship between PDE-7 inhibition and treatment of various diseases and disorders is well documented. *See, e.g.*, specification at paragraph [0008]. Thus, the level of predictability in the art, with respect to PDE-7 inhibition and treatment of, for example, T cell mediated immune diseases, is such that the effect of PDE-7 inhibition is

well known in the art and can be expected from compounds that exhibit PDE-7 inhibition.

Moreover, the Examiner has not indicated how the alleged unpredictability of *physiological activity* is relevant to the basis of the instant rejection, namely, that Applicants had not disclosed *a method of making* compounds of formula I "wherein R_1 is H, alkyl other than methyl or aryl." Office Action at 6.

Further, the Examiner referenced *In re Fisher,* as support for her position (*In re Fisher*, 427 F.2d 833, 166 U.S.P.Q. 18 (C.C.P.A. 1970)). *In re Fisher* describes a situation where an applicant for a patent disclosed the preparation of adrenocorticotrophic hormone (ACTH) to a potency of between 1.11 and 2.30 International Units of ACTH activity per milligram of tissue extract, such preparation being useful in the treatment of arthritis and other conditions. This level of potency was significantly higher than that achieved in prior art preparations of ACTH. The applicant attempted to claim an ACTH preparation having a potency of "at least 1 International Unit of ACTH per milligram." Thus, using the open-ended claim language "at least," the applicant attempted to claim his preparation more broadly than the specific embodiments disclosed in his specification. *Id.* at 839, 166 U.S.P.Q. at 23.

The issue before the court was whether the applicant "should be allowed to dominate *all* such compositions having potencies greater than 1.0, including future compositions having potencies far in excess of those obtainable from [applicant's] teachings plus ordinary skill." *Id.* at 839, 166 U.S.P.Q. at 24 (emphasis in original). The court held as follows:

> It is apparent that such an inventor should be allowed to dominate the future patentable inventions of others where

> those inventions were based in some way on his teachings. Such improvements, while unobvious from his teachings, are still within his contribution, since the improvement was made possible by his work. It is equally apparent, however, that he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence not in compliance with the first paragraph of 35 U.S.C. 112. That paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

Id.

The *Fisher* court, thus, concluded that while the applicant's disclosure provided one of ordinary skill in the art with sufficient guidance to prepare ACTH having *certain* potencies greater than 1 International Unit per milligram, it did not provide the requisite guidance for *all* potencies greater than 1. Accordingly, the claims were held unpatentable under § 112, first paragraph, because they did not "bear a reasonable correlation to" the scope of disclosure provided.

In contrast to *Fisher*, one of ordinary skill in the art would clearly understand, after reading the instant specification, how to prepare the compounds the Examiner alleges are not exemplified in the application. Therefore, the citation to *In re Fisher* does not support the instant rejection.

On the other hand, the holding in *In re Strahilevitz* clearly indicates that enablement is considered both in light of the disclosure in the specification and the state of the art. *In re Strahilevitz*, 668 F.2d 1229, 212 U.S.P.Q. 561 (C.C.P.A. 1982). In *In re Strahilevitz*, applicants sought to broadly claim a method and devices for removing haptens, antigens, and antibodies from blood. Their broadest method claim read as follows:

> An immunological method for removing from a living mammal a hapten in the blood of said mammal, comprising connecting in the blood circulatory system of said mammal a hapten-removing device, said device comprising passage means for said blood; an antibody to said hapten in said device; and exposure means in said device for exposing said hapten to said antibody and for preventing said antibody from entering said circulatory system.

Id. at 1230, 212 U.S.P.Q. at 561-62.

Applicants had described the invention with specificity, but had not disclosed even a single working example. The court acknowledged that the claims at issue were extremely broad. Yet the court reversed the Board's holding of nonenablement pointing out that § 112 does not require working examples (though they may be desirable in complex technologies). Because one of ordinary skill would have been able to carry our the invention based on the knowledge in the art, the *Strahilevitz* court found the broad claims enabled throughout their entire scope.

Fisher and *Strahilevitz* thus illustrate, at opposite ends of the enablement spectrum, the requirements of § 112 are satisfied if the disclosure reasonably apprises the ordinary artisan, in light of what is well-known in the art, how to make and how to use a claimed invention throughout its scope. The present situation favors *Strahilevitz* (i.e., the specification provides ample support to make and use compounds of the present invention) over *Fisher*, when one considers the *Wands* factors such as the teachings in the specification, the level of skill in the art, and the degree and scope of experimentation needed.

3. Direction or Guidance

The Examiner contends that the direction or guidance "provided is very limited." Office Action at 6. However, the instant specification provides detailed disclosure on

the synthesis including starting materials of the claimed compounds, as well as a procedure for determining pharmacological activity.

For example, the specification teaches a detailed synthesis of the claimed genus of compounds, detailed composition preparations, in addition to providing several non-limiting examples of synthesis of specific compounds, as well as demonstrating how the claimed compounds were analyzed post-synthesis including proton NMR, carbon NMR, LC-MS, elemental analysis, etc. *See* specification at paragraphs [0239]-[0244].

These paragraphs clearly teach how to prepare compounds of the invention wherein R_4 could be any of the radicals recited for R_4 in the claims, including H, an alkyl other than methyl or aryl. The Examiner has not explained how this disclosure fails to teach the preparation of compounds "wherein R_1 [sic, R_4] is H, alkyl other than methyl or aryl," on which this rejection is based.

Regarding the Examiner's belief that the specification fails to disclose the starting materials for compounds of the invention where R_4 is H, alkyl other than methyl or aryl, Applicants point out that the specification clearly discloses compounds of formula (II), which represent the starting materials for compounds wherein R_4 is any of the radicals recited for R_4 in the claims, including H, an alkyl other than methyl or aryl. *See, e.g.*, Specification at Scheme I immediately following ¶ [0240]. Moreover, the specification also indicates that the reaction depicted in Scheme I follows the teachings of GB 1 454 529 for the preparation of thienyl derivatives of formula (IV), which have an R_4 substituent, and which is further proof that all the necessary starting materials to synthesize the compounds of the invention are available to one of ordinary skill in the art. *Id.* at ¶ [241].

Further, the courts have pointed out that "[n]ot every last detail [of an invention need] be described [in a patent specification], else patent specifications would turn into production specifications, which they were never intended to be." *In re Gay*, 309 F.2d 769, 774, 135 U.S.P.Q. 311, 316 (C.C.P.A. 1962) (emphasis added). Citing the opinion in *Gay*, the Board of Patent Appeals and Interferences echoed this point in the statement that "the law does not require a specification to be a blueprint in order to satisfy the requirement for enablement under 34 U.S.C. 112, first paragraph," *Staehelin v. Secher*, 24 U.S.P.Q.2d 1513 (Bd. Pat. App. & Int. 1992). Indeed, a specification need not describe -- and best omits -- that which is well-known in the art. *See, e.g., In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991).

In summary, the specification provides more than adequate guidance or synthesis of the compound including the starting materials, as well as how to measure PDE-7 inhibition, in addition to the disclosed preparative examples and the specific species examples.

4. State of the Prior Art and Working Examples

The Examiner asserts that the disclosed compounds "are substituted thieno[2,3-d]pyrimidines of Formula I wherein R_4 = methyl which are well documented in the art." *Id.* at 2. To the extent the Examiner is implying that the compounds of the invention wherein R_4 = methyl were known in the art, Applicants respectfully disagree. Indeed, Applicants highlight the fact that the Examiner has not provided a single example of the supposed documentation indicating that the invention is anticipated.

The Examiner asserts on page 7 of the Office Action that there are "no working examples ... of Formula I wherein R_4 is H, an alkyl other than methyl or an aryl." *Id.*

Applicants respectfully point out that this is not the standard for enablement. The Federal Circuit has emphasized that "the specification [need not] necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art." *AK Steel Corp. v. Sollac,* 344 F.3d 1234, 1244 (Fed. Cir. 2003) (citations omitted).

The Examiner seems to construe the possible need for some experimentation to mean that there is a lack of enabling disclosure. However, the very case cited by the Examiner in her non-enablement argument explains:

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. *The key word is 'undue,' not 'experimentation.'*

In re Wands, 858 F.2d 731, 736-37 (Fed. Cir. 1988) (footnote and internal citations omitted, emphasis added). Consistent with this guidance, and as established above, the specification discloses detailed methods for the preparation of compounds of the invention wherein R_4 could be any of the radicals recited in the claims, including H, an alkyl other than methyl or aryl, as well as the necessary starting materials for the synthesis of the compounds of the invention. *See, e.g.,* specification at paragraphs [0239]-[0244].

In the present case, the 135 examples disclosed in the specification more than suffice a finding of enablement. This is especially true because those examples teach how to prepare compounds where R_4 is methyl (an alkyl group) and the Examiner has not explained why such information would not have been sufficient for the preparation of

compounds where R_4 is a hydrogen, another alkyl other than methyl, or aryl. *See, e.g.*, specification at Examples 1-135, and the additional "Preparations" 1 to 17. That is, the Examiner has not explained why one of ordinary skill in the art would not have been able to simply replace the methyl moiety corresponding to R_4 with either a hydrogen, an alkyl other than methyl, or an aryl group to prepare the compounds for which allegedly there is no synthesis disclosed, *especially in view of the express indication to do so in Scheme I of the specification. Id.* at ¶ [0240] to [0241].

5. Skill of those in the art and the quantity of experimentation needed

The Examiner states that "[s]ince there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome." *Id.* The Examiner misconstrues this factor and overreaches. Here, the specification, as discussed at several points hereinabove, provides substantial guidance to one skilled in the art with respect to preparing the starting materials, reacting the starting materials to obtain intermediates, and further react these intermediates to obatin the claimed compounds, with detailed experimental information including physical parameters required such as heating to specific temperatures, catalysts and solvents. *See, e.g.*, Specification at ¶¶ [0239] to [0240]. In addition, the specification provides a detailed pharmacological assay to determine PDE-7 inhibition activity of the claimed compounds. The mere fact that some experimentation may be required to synthesize specific compounds of the invention from the general teachings therein does not compel a finding of lack of enablement. *See Johns Hopkins Univ. v. CellPro, Inc.,* 152, F.3d 1342, 1360-61, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998).

Thus, while some experimentation may be arguably required to synthesize some specific compounds of the invention, one skilled in the art would be reasonably guided to the claimed invention by the disclosure of the specification. Such guidance is clearly implicated by the preparative and working examples provided in the specification.

For at least the foregoing reasons, Applicants maintain that proper consideration of the factors set forth in *Wands* weighs in favor of a conclusion that one skilled in the art would be able to make and use the invention commensurate in scope with the claims, without undue experimentation. Accordingly, Applicants submit that their disclosure is fully enabling and respectfully request that this rejection be withdrawn.

V. Rejection under 35 U.S.C. § 103(a)

Claims 1, 5-10 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over European Patent Application No. EP 1 329 454 A1 to Umeda et al. ("*Umeda*") for the reasons set forth at pages 7-9 of the Office Action. In particular, the Examiner contends that *Umeda* "teaches compounds of formula (I), wherein R_1=hydrogen, R_2=(3-chloro-4-methoxycyclohexyl)methylene, R_3=3-pyridyl and R_4=methyl." *See* Office Action at 8. Applicants respectfully disagree and traverse the rejection for at least the following reasons.

First, the compound the Examiner references in *Umeda* (page 14, Table 1, compound 4) does not comprise a "3-chloro-4-methoxy*cyclohexyl*" group as an R_2 substituent as alleged by the Examiner, rather, the R_2 substituent is a 3-chloro-4-methoxy*benzyl* group. *See e.g., Umeda*, Example 4 at p. 10; p.14, Table 1. Nowhere in the present application is R_2 defined as a substituted benzyl group so as to

encompass the relevant substituent of the compound singled out by the Examiner in *Umeda*.

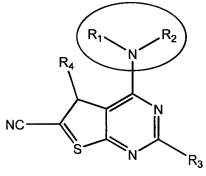
Further, the Examiner concludes that because "the reference teaches the substituents at the R_2 position of the bicycle can also be cyclohexylmethylene according to the genus of formula (I) of page 2 of the reference, last line ... [and] the reference teaches the R_3 substituent can be phenyl ... the reference renders said claims obvious." *Id.* at 9. Applicants respectfully disagree.

Although the Examiner cites to the *Graham v. John Deere* standard in the Office Action at page 8, the Examiner has failed to apply the standard to the instant facts. For example, the Examiner mentions an alleged similarity between the compounds of *Umeda* and the instant compounds, by arguing that both teach that the respective R_3 substituents can be phenyl. Office Action at 9. However, Applicants have failed to identify any disclosure in *Umeda* wherein R_3 can be phenyl. At best, R_3 in *Umeda* can be an amine substituted with phenyl [$N(r_1)$phenyl], or an acyl phenoxy [$(CH_2)_kC(=0)$-phenoxy], but not a phenyl. In any event, R_3 in the instant claims is neither directed to an amine substituted with phenyl nor an acyl phenoxy.

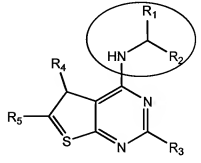
Moreover, the Examiner has not acknowledged the following ***differences*** between the present compounds and those of *Umeda*.

Compounds of the invention according to general formula (I) are different from those of *Umeda* at least at the moiety shown in the circle below.

Claimed Compound



Compound disclosed in Umeda



That group corresponds to, for the instantly claimed compounds, an amine group that can be a primary, secondary or tertiary amine group optionally substituted at R_1 and/or R_2, independently, from various groups. However, the amine group of the claimed compound of Umeda cannot be either a primary amine or a tertiary amine, but must always be a secondary amine group wherein R_1 is hydrogen or $C_{1\text{-}6}$ alkyl and R_2 is chosen from various groups. Only when R_2 in the instant claims is chosen to be, from among various other recited radicals, $-(CH_2)_n-G$, and n = 1, *and* G is a C_3-C_6 cycloalkyl group can the two groups be construed as *similar*. Nonetheless, such picking and choosing is prohibited in obviousness determinations. *See, e.g., In re Fine,* 5 U.S.P.Q.2d 1596, 1600, 837 F.2d 1071, 1075 (Fed. Cir. 1988).

Furthermore, the substituent on the thiophene portion of the claimed compound is recited to be a cyano group (*i.e.* a carbonitrile). However, *Umeda* discloses a broad definition for its similarly-placed R_5 substituent, that can be chosen from:

> cyano, phenyl optionally substituted with G_2, a saturated or unsaturated heterocyclic group containing 1 to 4 heteroatoms selected from among N, O and S and optionally substituted with G_3, or a group represented by Formula $(CH_2)_kC(=0)R_6$ or CH=CHC(=O)R6.

Umeda at page 3, lines 6-8. *Umeda* does not suggest that a cyano group in this position is particularly preferred, nor has the Examiner provided a reason why one of ordinary skill in the art would have chosen a cyano group, from among all other possibilities disclosed in *Umeda*, to produce a compound that may arguably be only *similar*, with respect to R_5, to those instantly claimed.

Although the Examiner asserts that the cited reference "renders said claims obvious," the Examiner seemed to have simply considered the "gist" of the invention, rather than properly analyzing in detail the differences of the instant compounds with the prior art. *See* M.P.E.P. § 2141.02(II).

Moreover, the Federal Circuit has recently applied the principles enunciated in the *KSR* decision and indicated that not only must the compounds be similar, but there must also be "a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention.'" *Takeda Chem. Ind., Ltd. v. Alphapharm Pty., Ltd.* 83 U.S.P.Q.2d 1169, 1174 (Fed. Cir. 2007) (citations omitted). Thus, "in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new compound." *Id.*

This holding necessarily requires that the Examiner: a) identify all of the differences between the prior art and the claimed invention, and then b) explain the reasons why one of ordinary skill in the art would have made such modifications. *The Examiner has complied with neither requisite.* Indeed, the Examiner has provided absolutely no arguments why one of ordinary skill in the art would have modified the compounds of the cited references in a manner necessary to arrive at the presently

claimed compounds of formula I, for example, suggesting at least all of the modifications mentioned above to bridge the gaps between the instant compounds and those of *Umeda*. Accordingly, for at least these reasons, the Examiner has failed to show a *prima facie* case of obviousness, and the Applicants respectfully request that this rejection be withdrawn.

VI. Conclusions

In view of the foregoing remarks, Applicants submit that the invention fully complies with the requirements of 35 U.S.C. §112 and is neither anticipated nor rendered obvious in view of the prior art references cited by the Examiner. Applicants therefore request the entry of this Response and Amendment, the Examiner's reconsideration of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: _____
Carlos M. Téllez
Reg. No. 48,638

Dated: May 20, 2008

Attachment: Copies for definition of acyl from Hawley's Condensed Chemical Dictionary (3 pages)